REMARKS

The Examiner is thanked for the thorough examination of the application. An article by NEVO et al. is appended to this paper.

Claims 1, 2 and 4-18 are pending in the application.

No new matter is believed to be added to the application by this amendment.

Entry of this response under 37 CFR §1.16 is respectfully requested because it raises no new issues and places the application in condition for allowance.

Rejection Under 35 USC §103(a)

Claims 1, 2, 4-6 and 8-18 have been rejected under 35 USC §103(a) as being unpatentable over SCHNEIDER et al. (Journal of Vascular Surgery). Traversal of this rejection is respectfully maintained for at least the reasons set forth below.

Independent claims 1 and 12 of the present invention recite a synthetic coating or composition that includes 50-97% heparan sulfate, 1-20% laminin and 0.2-15% type IV collagen.

SCHNEIDER et al. has been discussed in previous responses.

As as been noted, there is no disclosure whatsoever in SCHNEIDER et al. that the constituents of the present invention are present in the synthetic coating at the specific claimed concentrations.

The article by SCHNEIDER et al. clearly does not describe a synthetic coating, but instead describes a naturally produced coating. Moreover, there is no disclosure whatsoever in SCHNEIDER et al. that the consitituents according to the present invention are present in the specific claimed concentrations of the present invention.

More specifically, SCHNEIDER et al. fail to disclose the use of heparan sulphate (50% or greater) as a major component in the synthetic coating in order to prevent thrombosis. Therefore independent claims 1 and 12 of the present invention are clearly patentable over SCHNEIDER et al.

Furthermore, in view of the ***natural*** nature of the related art coatings, the skilled person would not interfere with nature in order to vary the amounts of the constituents in this coating, specifically to reach the amounts according to the present invention.

On page 655, left column, last paragraph, SCHNEIDER et al. demonstrate the importance of the natural nature of the coating, because the "***naturally*** produced ECM" supposedly has "superior cell growth-promoting properties" when compared with "isolated constituents of the ECM". Therefore, SCHNEIDER et al. teaches away from using a coating with specifically selected substituents departing from nature.

Moreover, SCHNEIDER et al. is concerned with a coating that improves adhesion and growth of ECs on synthetic graft

material. In practice, the bare coating of SCHNEIDER et al. appears to have a proliferative effect with an enhanced probability of thrombosis. Not surprisingly, Schneider teaches to expose the coating to glutaraldehyde or to seed vascular ECs to the coating to create a nonthrombogenic surface to prevent thrombosis. There is no disclosure or suggestion in SCHNEIDER et al. to modify the ECM in an attempt to improve the anti-thrombotic properties.

In the Response to Arguments the Official Action asserts that SCHNEIDER et al. uses an ECM, the constituents of which are the same as those claimed by the present invention and that natural or synthetic, the composition appears to be the same with a reasonable degree of modification.

However, in addition to the previous distinctions over SCHNEIDER et al. of record, please find attached a document by NEVO et al. in which the proteoglycan content of extracellular matrix (ECM) produced by bovine corneal endothelial cells is examined.

According to NEVO et al. the total amount of proteoglycans in the ECM is 5% to 6% dry weight percentage (see for example the abstract, p.51 first sentence or p.55 second paragraph).

Of this total amount of proteoglycans in the ECM only 50% is heparan sulfate (see p.55 third paragraph). Thus, the ECM

produced by bovine corneal endothelial cells comprises a mere 3% heparan sulfate.

In contrast, the present invention is concerned with a synthetic coating having heparan sulfate as main constituent in a range of 50-97%. lt was found that this coating has an improved anti-thrombogenic effect over the known coatings for intraluminal devices.

None of the cited prior art typified by SCHNEIDER et al. disclose or suggest such a coating for an intraluminal device suitable for implantation in the human body.

That is, the SCHNEIDER et al. reference is concerned with a natural coating formed from an ECM produced specifically by bovine corneal endothelial cells as described in the document by NEVO et al. There is no disclosure or suggestion whatsoever in Schneider that the constituents according to the present invention are present in the coating in the specific concentrations as taught by the invention. More specifically, there is no disclosure or suggestion in SCHNEIDER et al. that the coating having heparan sulfate as main constituent in range of 50-97%. Contrarily, the coating is approximately 3% heparan sulfate, as evidenced by NEVO et al.

Furthermore, the skilled artisan does not find any hint in SCHNEIDER et al. to a coating formed from heparan sulfate as main constituent in a non-natural range of 50-97%. In fact, SCHNEIDER et al. argue against the use of such a synthetic

coating, since according to Schneider "*the naturally produced ECM has superior cell growth-promoting properties as compared with isolated constituents*".

As a result, one of ordinary skill and creativity in the art would not be motivated by SCHNEIDER et al. to produce claim 1 of the present invention. A *prima facie* case of unpatentability has not been made. Claims depending upon claim 1 are patentable over SCHNEIDER et al. for at least the above reasons.

This rejection is believed to be overcome, and withdrawal thereof is respectfully requested.

Rejection Under 35 USC §112, First Paragraph

Claims 1-18 have been rejected under 35 USC §112, first paragraph as failing to comply with the written description requirement. This rejection is respectfully traversed.

The Official Action asserts that the claims set forth a "synthetic" composition that is not disclosed in the original specification, taking the position that the preparation of a composition as recited at page 6, line 20 of the specification is not adequate support, since even natural compositions such as those used in bone growth, must first treat the natural composition to isolate the desired product.

However, the claims of the present invention are concerned with a synthetic coating containing 50-97% heparan sulfate. A naturally produced coating, i.e., a naturally

produced ECM, contains a relatively low amount heparin sulfate, as evidenced by NEVO et al. None of the cited prior art documents discloses or suggests a naturally produced ECM containing heparan sulfate in the range of 50-97%.

Therefore a coating comprising 50-97% heparan sulfate, which concentration is far removed from naturally occurring concentrations of heparan sulfate, will be understood by the skilled artisan to be non-natural, i.e., synthetic.

Also note the dependent claims, which claim antibiotics for example, which clearly would not arise from a natural sample.

Therefore it is deemed that the claims do comply with the written description requirement.

This rejection is believed to be overcome, and withdrawal thereof is respectfully requested.

Conclusion

The rejections have been overcome, obviated or rendered moot. No issues remain. The Examiner is accordingly respectfully requested to place the application in condition for allowance and to issue a Notice of Allowability.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON

/Robert E. Goozner/

Robert E. Goozner, Reg. No. 42,593
Customer No. 00466
209 Madison Street, Suite 500
Alexandria, VA 22314
Telephone (703) 521-2297
Telefax (703) 685-0573
(703) 979-4709

REG/lad

Attachment: NEVO et al., *Connective Tissue Research*, 1984, Vol. 13, pp. 45-57